WE CLAIM:

1. A method for generation of a small fluid volume, containing a moiety of interest for crystallization and having a known composition, comprising acoustically depositing one or more reagent-containing fluid droplets at a site on a substrate surface, wherein at least one of the reagent-containing fluid droplets deposited at the site contains the moiety of interest for crystallization and at least one of the reagent-containing fluid droplets contains an agent that increases the likelihood of crystal formation.

2. The method of claim 1 further comprising detecting whether the moiety of interest for crystallization has formed crystals.

3. The method of claim 1 wherein an array of small fluid volumes each having a known composition and known chemical and physical conditions is generated on the substrate surface.

4. The method of claim 1 wherein at least one of the reagent-containing fluid droplets deposited at the site contains one or more crystallization-promoting agents selected from the group consisting of inorganic salts, inorganic molecules, organic salts, organic non-polymeric molecules, and polymers.

5. The method of claim 4 wherein the crystallization-promoting agent is a surfactant or chaotropic agent.

6. The method of claim 1 wherein the moiety of interest for crystallization is solubilized by a surfactant or chaotropic agent.

7. The method of claim 4 wherein the moiety of interest for crystallization is solubilized by a surfactant or chaotropic agent.

8. The method of claim 1 or 4 wherein the moiety of interest for crystallization is stabilized in a specific conformation by a ligand.

9. The method of claim 1 wherein the moiety of interest for crystallization comprises a biomacromolecule.

10. The method of claim 4 wherein the moiety of interest for crystallization comprises a biomacromolecule, wherein the biomacromolecule is stabilized in a specific conformation by a ligand selected from the group consisting of ions, non-polymeric molecules, and biopolymers.

11. The method of claim 10 wherein the ligand comprises a divalent cation, a steroid, a retinoid, or a biopolymer comprising a sequence of monomers, the monomers selected from the group consisting of monosaccharides, amino acids, and nucleotides.

12. The method of claim 10 wherein the ligand is an ionic constituent of a salt that functions as a crystallization-promoting agent.

13. The method of claim 6 wherein the surfactant or chaotropic agent that solubilizes the moiety of interest is a crystallization-promoting agent.

14. The method of claim 6 wherein the moiety of interest comprises a biomacromolecule, and the surfactant or chaotropic agent that solubilizes the biomacromolecule is a crystallization-promoting agent.

15. The method of claim 1, 2, 3, 6, or 10 wherein the moiety of interest comprises a biomacromolecule comprising a partially or fully native protein domain.

16. The method of claim 15 wherein the biomacromolecule comprises a fully or partly native protein.

17. The method of claim 1, 2, 3, or 6 wherein the moiety of interest comprises a partially native protein domain.

18. The method of claim 17 wherein the moiety of interest additionally comprises a fully denatured protein domain.

19. The method of claim 18 wherein the biomacromolecule additionally comprises a fully denatured protein domain.

20. The method of claim 17 wherein the moiety of interest additionally comprises a fully denatured protein domain and a native protein domain.

21. The method of claim 10 wherein at least one of the reagent-containing fluid droplets deposited at the site contains a second biomacromolecule.

22. The method of claim 6 further comprising means for detecting whether the moiety of interest for crystallization has formed crystals.

23. The method of claim 8 further comprising means for detecting whether the moiety of interest for crystallization has formed crystals.

24. The method of claim 10 further comprising means for detecting whether the moiety of interest for crystallization has formed crystals.

25. The method of claim 6 wherein an array of small fluid volumes each having a different known composition and different known chemical and physical conditions is generated on the substrate surface.

26. The method of claim 8 wherein an array of small fluid volumes each having a different known composition and different known chemical and physical conditions is generated on the substrate surface.

27. The method of claim 10 wherein an array of small fluid volumes each having a different known composition and different known chemical and physical conditions is generated on the substrate surface.

28. The method of claim 1, 2, or 3 further comprising controlling temperature of the substrate and ambient temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

29. The method of claim 4 or 6 further comprising detecting whether the moiety of interest for crystallization has formed crystals and controlling the temperature of the substrate and ambient gas temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

30. The method of claim 8 further comprising detecting whether the moiety of interest for crystallization has formed crystals and controlling temperature of the substrate and ambient gas temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

31. The method of claim 10 further comprising detecting whether the biomacromolecule has formed crystals and controlling temperature of the substrate and

ambient gas temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

32. The method of claim 3 further comprising detecting whether the moiety of interest for crystallization has formed crystals and controlling temperature of the substrate and ambient gas temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

33. The method of claim 3 wherein at least one of the reagent-containing fluid droplets deposited at the site contains one or more crystallization promoting agents selected from the group consisting of inorganic salts, organic salts, organic non-polymeric molecules, and polymers.

34. The method of claim 33 wherein the crystallization-promoting agent is a surfactant or chaotropic agent.

35. The method of claim 33 wherein the moiety of interest for crystallization is solubilized by a surfactant or chaotropic agent.

36. The method of claim 35 wherein the moiety of interest for crystallization is stabilized in a specific conformation by a ligand selected from the group consisting of ions, non-polymeric molecules, and biopolymers.

37. The method of claim 36 further comprising detecting whether the moiety of interest for crystallization has formed crystals and controlling temperature of the substrate and ambient gas temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

38. The method of claim 2 wherein the detecting is acoustic detecting.

39. The method of claim 37 wherein the detecting is acoustic detecting.

40. The method of claim 39, wherein each small fluid volume contains polyethylene glycol and dimethyl sulfoxide.

41. The method of claim 1 wherein the moiety of interest for crystallization is a biomacromolecule and both the small fluid volume and the reagent-containing droplets have a volume of up to about 1 microliter.

42. The method of claim 41, wherein the moiety of interest for crystallization is a biomacromolecule and the small fluid volume has a volume of about 1 picoliter to 30 nanoliters and the reagent-containing droplets have a volume of about 0.1 picoliter to 10 nanoliters.

43. A method for generation of a small fluid volume, the small fluid volume containing a moiety of interest for crystallization and having a known composition, and determining whether the known composition in combination with known chemical and physical conditions favor crystallization of the moiety of interest, the method comprising the steps:

(a) depositing one or more reagent-containing fluid droplets at a site on a substrate surface by focused energy ejection, at least one of the reagent-containing fluid droplets deposited at the site containing the moiety of interest for crystallization; and

(b) detecting the presence and quantity of crystalline material composed of the moiety of interest in the small fluid volume at the site.

44. The method of claim 43 further comprising:

(c) depositing by focused energy ejection one or more reagent-containing fluid droplets at a site on a substrate surface having a small fluid volume previously deposited at the site; and

(d) detecting for the presence and amount of crystals of the moiety of interest in the small fluid volume at the site.

45. The method of claim 44 wherein said detecting of steps (b) and (d) further comprises periodic detection of the amount and size of crystals

46. The method of claim 43 or 45 wherein said detecting is acoustic.

47. The method of claim 46 wherein an array of small fluid volumes each having a known composition and a known chemical and physical conditions are generated on the substrate surface.

48. The method of claim 43 wherein at least one of the reagent-containing fluid droplets deposited at the site contains one or more crystallization promoting agents selected from the group consisting of inorganic salts, organic salts, organic non-polymeric molecules, and polymers.

49. The method of claim 47 wherein the crystallization-promoting agent is a surfactant or chaotropic agent.

50. The method of claim 43 wherein the moiety of interest for crystallization is solubilized by a surfactant or chaotropic agent.

51. The method of claim 48 wherein the moiety of interest for crystallization is solubilized by a surfactant or chaotropic agent.

52. The method of claim 43 or 50 wherein the moiety of interest for crystallization is a biomacromolecule, the biomacromolecule being stabilized in a specific conformation by a ligand selected from the group consisting of ions, non-polymeric molecules, and biopolymers.

53. The method of claim 52 wherein the ligand comprises a divalent cation, a steroid, a retinoid, or a biopolymer comprising a sequence of monomers, the monomers selected from the group consisting of monosaccharides, amino acids, and nucleotides.

54. The method of claim 52 wherein the ligand is an ionic constituent of a salt that functions as a crystallization-promoting agent.

55. The method of claim 52 wherein the surfactant or chaotropic agent that solubilizes the biomacromolecule is a crystallization-promoting agent.

56. The method of claim 52 wherein the biomacromolecule comprises a partially or fully native protein domain.

57. The method of claim 56 wherein the moiety of interest comprises a native protein.

58. The method of claim 55 wherein the biomacromolecule comprises a partially or fully native protein.

59. The method of claim 43 wherein the moiety of interest comprises a native protein or partially denatured protein.

60. The method of claim 59 wherein the moiety of interest additionally comprises a native protein domain.

61. The method of claim 59 wherein the moiety of interest additionally comprises a fully denatured protein domain.

62. The method of claim 59 wherein the moiety of interest additionally comprises a fully denatured protein domain and a native protein domain.

63. The method of claim 52 wherein at least one of the reagent-containing fluid droplets deposited at the site additionally contains a polypeptide.

64. The method of claim 50 further comprising means for detecting whether the polypeptide of interest for crystallization has formed crystals.

65. The method of claim 50 wherein an array of small fluid volumes each having a known composition and known chemical and physical conditions are generated on the substrate surface.

66. The method of claim 43 or 45 wherein said detecting is acoustic detection.

67. The method of claim 66 further comprising independently controlling temperature of the substrate and ambient temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

68. The method of claim 48 further comprising controlling the temperature of the substrate and ambient gas temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

69. The method of claim 47 further comprising controlling temperature of the substrate.

70. The method of claim 47 wherein at least one of the reagent-containing fluid droplets deposited at the site contains one or more crystallization promoting agents selected from the group consisting of inorganic salts, inorganic molecules, organic salts, organic non-polymeric molecules, and polymers.

71. The method of claim 70 wherein the moiety of interest for crystallization is a biomacromolecule, wherein the biomacromolecule is stabilized in a specific conformation by a ligand selected from the group consisting of ions, non-polymeric molecules and biopolymers.

72. The method of claim 71 further comprising independently controlling temperature of the substrate and ambient gas temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

73. The method of claim 45 wherein the detecting is acoustic detecting.

74. The method of claim 72 wherein the detecting is acoustic detecting.

75. The method of claim 72 wherein each small fluid volume contains polyethylene glycol and dimethyl sulfoxide.

76. The method of claim 75 wherein the small fluid volume has a volume of about 1 picoliter to 30 nanoliters and the reagent-containing droplets have a volume of about 0.1 picoliter to 10 nanoliters.

77. The method of claim 45 wherein the moiety of interest for crystallization is a biomacromolecule, the small fluid volume has a volume of about 1 picoliter to 30 nanoliters and the reagent-containing droplets have a volume of about 0.1 picoliter to 10 nanoliters.

78. A method for generation of a small fluid volume containing a biomacromolecule of interest for crystallization and having a known composition and known chemical and physical conditions comprising acoustically depositing one or more reagent-containing fluid droplets at a site on a substrate surface, at least one of the reagent-containing fluid droplets deposited at the site containing the biomacromolecule of interest for crystallization.

79. The method of claim 78 further comprising detecting whether the biomacromolecule of interest for crystallization has formed crystals.

80. The method of claim 78 wherein an array of small fluid volumes each having a known composition and known chemical and physical conditions is generated on the substrate surface.

81. The method of claim 78 wherein at least one of the reagent-containing fluid droplets deposited at the site contains one or more crystallization promoting agents selected from the group consisting of inorganic salts, organic salts, organic non-polymeric molecules, and polymers.

82. The method of claim 81 wherein the crystallization-promoting agent is a surfactant or chaotropic agent.

83. The method of claim 81 wherein the biomacromolecule of interest for crystallization is solubilized by a surfactant or chaotropic agent.

84. The method of claim 81 or 83 wherein the biomacromolecule of interest for crystallization is stabilized in a specific conformation by a ligand selected from the group consisting of ions, non-polymeric molecules, and biopolymers.

85. The method of claim 84 wherein the ligand comprises a divalent cation, a steroid, a retinoid, or a biopolymer comprising a sequence of monomers, the monomers selected from the group consisting of monosaccharides, amino acids, and nucleotides.

86. The method of claim 84 wherein the ligand is an ionic constituent of a salt that functions as a crystallization-promoting agent.

87. The method of claim 83 wherein the surfactant or chaotropic agent that solubilizes the biomacromolecule of interest is a crystallization-promoting agent.

88. The method of claim 78 wherein the biomacromolecule of interest comprises a native protein domain or a partially denatured protein domain.

89. The method of claim 88 wherein the biomacromolecule of interest comprises a native protein.

90. The method of claim 78 wherein the biomacromolecule of interest for crystallization comprises a nucleic acid.

91. The method of claim 88 wherein the nucleic acid has a conformation.

92. The method of claim 78 wherein the biomacromolecule of interest comprises a partially native protein domain.

93. The method of claim 92 wherein the biomacromolecule of interest additionally comprises a native protein domain.

94. The method of claim 92 wherein the biomacromolecule of interest additionally comprises a fully denatured protein domain.

95. The method of claim 92 wherein the biomacromolecule of interest additionally comprises a fully denatured protein domain and a native protein domain.

96. The method of claim 84 wherein at least one of the reagent-containing fluid droplets deposited at the site contains a second biomacromolecule.

97. The method of claim 84 further comprising means for detecting whether the biomacromolecule of interest for crystallization has formed crystals.

98. The method of claim 84 wherein an array of small fluid volumes each having a known composition and known chemical and physical conditions is generated on the substrate surface.

99. The method of claim 79 or 80 further comprising controlling temperature of the substrate and ambient temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

100. The method of claim 84 further comprising detecting whether the biomacromolecule of interest for crystallization has formed crystals.

101. The method of claim 100 further comprising independently controlling temperature of the substrate and ambient gas temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

102. The method of claim 80 further comprising detecting whether the biomacromolecule of interest for crystallization has formed crystals and controlling temperature of the substrate and ambient gas temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

103. The method of claim 80 wherein at least one of the reagent-containing fluid droplets deposited at the site contains one or more crystallization promoting agents selected from the group consisting of inorganic salts, inorganic molecules, organic salts, organic non-polymeric molecules, and polymers.

104. The method of claim 103 wherein the biomacromolecule of interest for crystallization is solubilized by a surfactant or chaotropic agent.

105. The method of claim 80 or 104 wherein the biomacromolecule of interest for crystallization is stabilized in a specific conformation by a ligand selected from the group consisting of ions, non-polymeric molecules, and biopolymers.

106. The method of claim 105 further comprising detecting whether the biomacromolecule of interest for crystallization has formed crystals and controlling temperature of the substrate and ambient gas temperature and pressure surrounding the reagent-containing droplets and the small fluid volumes.

107. The method of claim 79 wherein the detecting is acoustic detecting.

108. The method of claim 106 wherein the detecting is acoustic detecting.

109. The method of claim 106 wherein each small fluid volume contains polyethylene glycol and dimethyl sulfoxide.

110. The method of claim 78, 79, or 80 wherein the biomacromolecule comprises a peptidic biopolymer selected from the group consisting of oligopeptides and polypeptides.

111. The method of claim 78, 79, or 80 wherein the biomacromolecule comprises a nucleotidic biopolymer selected from the group consisting of oligonucleotides and polynucleotides.

112. The method of claim 110 wherein the biomacromolecule additionally comprises a saccharidic biopolymer selected from the group consisting of oligosaccharides and polysaccharides.

113. The method of claim 78 wherein the small fluid volume has a volume of about 1 picoliter to 30 nanoliters and the reagent-containing droplets have a volume of about 0.1 picoliter to 10 nanoliters.

114. The method of claim 78 wherein at least one of the reagent-containing fluid droplets deposited at the site contains two or more immiscible phases.

115. The method of claim 114 wherein the immiscible phases comprise an aqueous fluid and a phospholipid and the ejected droplets comprise the biomacromolecule of interest for crystallization embedded or anchored in a phospholipid micelle or a phospholipid bilayer.

116. A method for ejecting a different reagent-containing fluid from each of a plurality of fluid reservoirs toward designated sites on a substrate surface to form a combinatorial array of fluid droplets containing a biomacromolecule of interest for crystallization, the method comprising the steps:

(a) positioning an acoustic ejector so as to be in acoustically coupled relationship to a first reservoir containing a first reagent-containing fluid;

(b) activating the ejector to generate acoustic radiation having a focal point near the surface of the first fluid, thereby ejecting a first droplet of the first reagent-containing fluid from the first reservoir toward a first designated site on the substrate surface, whereby the droplet adheres to the designated site;

(c) repositioning the ejector so as to be in acoustically coupled relationship to a second reservoir containing a second reagent-containing fluid different from the first;

(d) activating the ejector as in step (b) to eject a second droplet of the second reagent-containing fluid from the second reservoir toward the first designated site on the substrate surface, whereby the second droplet adheres to the designated site and mixes with the first droplet;

(e) repeating steps (c) and (d) with additional reservoirs each containing a different reagent-containing fluid until the first designated site on the substrate surface has a small fluid volume adhering thereto; and

(f) repeating steps (a) through (e) for the remaining designated sites of the array until each site has a small fluid volume adhering thereto,

wherein each small fluid volume contains the biomacromolecule of interest for crystallization in the droplets of the reagent-containing fluid, each small fluid volume occupying a designated site whereby the small fluid volumes are arrayed on the substrate surface at the designated sites and the composition and chemical conditions at each site are known from the steps of the method and the reagent-containing fluids deposited.

117. The method of claim 116 further comprising repeating steps (a) through (f) to alter the composition of the small fluid volume at each designated site.

118. The method of claim 117 further comprising controlling the physical conditions of the substrate and ambient gas physical conditions surrounding the fluid droplets and the small fluid volumes.

119. The method of claim 118 wherein the physical conditions controlled are temperature of the substrate and ambient gas temperature and pressure surrounding the fluid droplets and the small fluid volumes.

120. The method of claim 118 further comprising detecting crystallization of the biomacromolecule of interest.

121. The method of claim 120 wherein the detecting is by acoustic detection.

122. The method of claim 116 wherein at least one of the reagent-containing fluid droplets deposited at the site contains two or more immiscible phases.

123. The method of claim 116 wherein the immiscible phases comprise an aqueous fluid and a phospholipid and the ejected droplets comprise the biomacromolecule of interest for crystallization embedded or anchored in a phospholipid micelle or a phospholipid bilayer.

124. A system for combinatorial experiments to crystallize a moiety of interest and detect crystallization of the moiety of interest, the system comprising:

a plurality of sites arrayed on a substrate;

a plurality of reservoirs each adapted to contain a reagent-containing fluid;

an ejector comprising an acoustic radiation generator for generating acoustic radiation and a focusing means for focusing the acoustic radiation at a focal point near the fluid surface in each of the reservoirs; and

a means for positioning the ejector in acoustic coupling relationship to each of the reservoirs; and

means for detecting crystallization of the moiety of interest; wherein

one or more of the materials arrayed on the substrate are contacted with one or more reagent-containing fluids by acoustic ejection, and any physical or chemical change detected at a site upon said contacting denotes a screening result for the material present at said site contacted with said one or more reagent-containing fluids.

125. The system of claim 124 wherein the moiety of interest is a biomacromolecule.

126. The system of claim 124, wherein for said plurality of sites arrayed on the substrate, the sites are present at a density of from about 1,000 to about 100,000,000 sites per square centimeter.

127. The system of claim 124 wherein the means for detecting is acoustic detection.

128. The system of claim 124 further comprising means for ascertaining the quality of the crystals.

129. The system of claim 126 wherein the means for ascertaining the quality of the crystals is by x-ray diffraction or scanning diffractometry.

130. A spatial array comprising a plurality of small fluid volumes having a known composition and known chemical and physical condition on a substrate surface divided into a plurality of discrete surface sites, each site containing one small fluid volume residing in a localized region of the site, wherein each small fluid volume contains a moiety of interest for crystallization and the different sites are present at a density of from about 1,000 to about 1,500,000 sites per square centimeter.

131. The array of claim 130 wherein the moiety of interest for crystallization is a biomacromolecule.

132. The array of claim 130, wherein said substrate surface comprises a polymer.

133. The array of claim 130, wherein said substrate surface comprises an amorphous, crystalline, or molecular material.

134. The array of claim 130, wherein said substrate surface comprises a non-porous, impermeable material.

135. The array of claim 130, wherein said substrate surface comprises a porous, permeable material.

136. The array of claim 130 wherein a small fluid volume contains one or more crystallization promoting agents selected from the group consisting of inorganic salts, organic salts, organic non-polymeric molecules, and polymers.

137. The array of claim 136 wherein the crystallization-promoting agent is a surfactant or chaotropic agent.

138. The array of claim 136 wherein the biomacromolecule of interest for crystallization is solubilized by a surfactant or chaotropic agent.

139. The array of claim 136 wherein the biomacromolecule of interest for crystallization is stabilized in a specific conformation by a ligand selected from the group consisting of ions, non-polymeric molecules, and biopolymers.

140. The array of claim 139 wherein the ligand comprises a divalent cation, a steroid, a retinoid, or a biopolymer comprising a sequence of monomers, the monomers selected from the group consisting of monosaccharides, amino acids, and nucleotides.

141. The array of claim 139 wherein the ligand is an ionic constituent of a salt that functions as a crystallization-promoting agent.

142. The array of claim 130 wherein each of the plurality of small fluid volumes and the reagent-containing droplets have a volume of up to about 1 microliter.

143. The array of claim 142 wherein each of the plurality of small fluid volumes has a volume of about 1 picoliter to 30 nanoliters and the reagent-containing droplets have a volume of about 0.1 picoliter to 10 nanoliters.

144. A method for detecting crystals in a fluid comprising emitting focused acoustic energy having a focal point in the fluid and detecting the acoustic properties at the focal point,

wherein crystals are detected by differences in acoustic properties from the fluid.

145. The method of claim 144 wherein the focal point is scanned through the fluid.

146. The method of claim 144 wherein the acoustic properties are acoustic impedance or acoustic attenuation.

147. The method of claim 144 further comprising distinguishing crystals from precipitates by differences in acoustic properties therebetween.

148. The method of claim 144 further comprising distinguishing biomacromolecule crystals from non-biomacromolecule crystals by differences in acoustic properties therebetween.

149. The method of claim 145 wherein crystal size is determined.

150. The method of claim 149, further comprising periodic detection of quantity and size of crystals for determining kinetics of crystal nucleation and growth.